

NIH EXPLORATORY/DEVELOPMENTAL RESEARCH GRANT AWARD (R21)

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National Institute on Deafness and Other Communication Disorders (NIDCD)

(<http://www.nidcd.nih.gov/>)

National Institute on Drug Abuse (NIDA)

(<http://www.nida.nih.gov/>)

National Center for Research Resources (NCRR)

(<http://www.ncrr.nih.gov/>)

National Eye Institute (NEI)

(<http://www.nei.nih.gov/>)

National Institute on Aging (NIA)

(<http://www.nia.nih.gov/>)

National Institute on Alcohol Abuse and Alcoholism (NIAAA)

(<http://www.niaaa.nih.gov/>)

National Institute of Allergy and Infectious Diseases (NIAID)

(<http://www.niaid.nih.gov/default.htm>)

National Institute of Biomedical Imaging and Bioengineering (NIBIB)

(<http://www.nibib1.nih.gov/>)

National Institute of Child Health and Human Development (NICHD)

(<http://www.nichd.nih.gov/>)

National Institute of Dental and Craniofacial Research (NIDCR)

(<http://www.nidcr.nih.gov/>)

National Institute of Environmental Health Sciences (NIEHS)

(<http://www.niehs.nih.gov/>)

National Institute of Mental Health (NIMH)

(<http://www.nimh.nih.gov/>)

National Institute of Neurological Disorders and Stroke (NINDS)

(<http://www.ninds.nih.gov/>)

National Library of Medicine (NLM)

(<http://www.nlm.nih.gov/>)

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THIS PA CONTAINS THE FOLLOWING INFORMATION

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PURPOSE OF THIS PA

This announcement redefines the National Institutes of Health (NIH) Exploratory/Developmental Research Grant Award (R21) mechanism, and extends its use as an investigator-initiated mechanism to the Institutes and Centers (ICs) listed above. The R21 is intended to encourage exploratory and developmental research projects by providing support for the early and conceptual stages of these projects. The characteristics, requirements, preparation, and review criteria for the R21 application are described.

Investigators wishing to apply for an R21 grant should be aware that not all ICs accept investigator-initiated R21 applications. Investigators are strongly encouraged to consult the R21 website at <http://grants.nih.gov/grants/funding/r21.htm> to identify participating ICs and relevant programmatic areas. Consultation with NIH staff listed on the website is also encouraged. ICs that do not accept investigator-initiated R21 applications may also solicit R21 applications to meet specific program needs. Information related to the use of R21 awards by ICs that do not participate in this program is also listed on the R21 website. Additional information about special initiatives can be found in the NIH Guide for Grants and Contracts at <http://grants.nih.gov/grants/guide/index.html#search>, on IC websites, and through consultation with NIH staff. All investigator-initiated exploratory/developmental grant applications described in this announcement will be assigned to ICs according to standard PHS referral guidelines and specific program interests.

RESEARCH OBJECTIVES

The evolution and vitality of the biomedical sciences require a constant infusion of new ideas, techniques, and points of view. These may differ substantially from current thinking or practice and may not yet be supported by substantial preliminary data. By using the R21 mechanism, the NIH seeks to foster the introduction of novel scientific ideas, model systems, tools, agents, targets, and technologies that have the potential to substantially advance biomedical research.

The R21 mechanism is intended to encourage new exploratory and developmental research projects. For example, such projects could assess the feasibility of a novel area of investigation or a new experimental system that has the potential to enhance health-related research. Another example could include the unique and innovative use of an

existing methodology to explore a new scientific area. These studies may involve considerable risk but may lead to a breakthrough in a particular area, or to the development of novel techniques, agents, methodologies, models or applications that could have major impact on a field of biomedical, behavioral, or clinical research.

Applications for R21 awards should describe projects distinct from those supported through the traditional R01 mechanism. For example, long-term projects, or projects designed to increase knowledge in a well-established area will not be considered for R21 awards. Applications submitted under this mechanism should be exploratory and novel. These studies should break new ground or extend previous discoveries toward new directions or applications. Projects of limited cost or scope that use widely accepted approaches and methods within well established fields are better suited for the R03 small grant mechanism. Information on the R03 program can be found at <http://grants.nih.gov/grants/funding/r03.htm>.

MECHANISM OF SUPPORT

Applicants responding to this PA must use the NIH Exploratory/Developmental Research Grant (R21) award mechanism. The applicant will be solely responsible for planning, directing, and executing the proposed project.

The applicant may request a project period of up to two years with a combined budget for direct costs of up to \$275,000 for the two year period. For example, the applicant may request \$100,000 in the first year and \$175,000 in the second year. The request should be tailored to the needs of the project. Normally, no more than \$200,000 may be requested in any single year.

This PA uses just-in-time concepts. It also uses the modular budgeting format. (see <http://grants.nih.gov/grants/funding/modular/modular.htm>). All applications submitted in response to this announcement must use the modular budget format. This program does not require cost sharing as defined in the current NIH Grants Policy Statement at http://grants.nih.gov/grants/policy/nihgps_2001/part_i_1.htm.

Exploratory/developmental grant support is for new projects only; competing continuation applications will not be accepted. Two revisions of a previously reviewed exploratory/developmental grant application may be submitted as defined in NIH Policy at <http://grants.nih.gov/grants/policy/amendedapps.htm>.

ELIGIBLE INSTITUTIONS

Applications may be submitted by institution with any of the following characteristics:

- o For-profit or non-profit organizations
- o Public or private institutions, such as universities, colleges, hospitals, and laboratories
- o Units of State and local governments
- o Eligible agencies of the Federal government

- o Domestic or foreign
- o Faith-based or community-based organizations

INDIVIDUALS ELIGIBLE TO BECOME PRINCIPAL INVESTIGATORS

Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.

WHERE TO SEND INQUIRIES

The NIH encourages inquiries concerning this PA and welcomes the opportunity answer questions from potential applicants. Participating ICs and their contacts are listed at <http://grants.nih.gov/grants/funding/r21.htm>.

SUBMITTING AN APPLICATION

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). The PHS 398 is available at <http://grants.nih.gov/grants/funding/phs398/phs398.html> in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

APPLICATION RECEIPT DATES: Beginning with the June 1, 2003 receipt date, applications submitted in response to this program announcement will be accepted at the standard application deadlines, which are available at <http://grants.nih.gov/grants/dates.htm>. Application deadlines are also indicated in the PHS 398 application kit.

SUPPLEMENTAL INSTRUCTIONS: All instructions for the PHS 398 (rev. 5/2001) must be followed, with these exceptions:

- o Research Plan

Items a - d of the Research Plan (Specific Aims, Background and Significance, Preliminary Studies, and Research Design and Methods) may not exceed a total of 15 pages. No preliminary data is required but may be included if it is available. Please note that a Progress Report is not needed; competing continuation applications for an exploratory/developmental grant will not be accepted.

Appendix. Use the instructions for the appendix detailed in the PHS 398 except that no more than 5 manuscripts, previously accepted for publication, may be included.

SPECIFIC INSTRUCTIONS FOR MODULAR GRANT APPLICATIONS: All investigator initiated R21 applications must be submitted in a modular grant format. The

modular grant format simplifies the preparation of the budget in these applications by limiting the level of budgetary detail. Applicants request direct costs in \$25,000 modules. Section C of the research grant application instructions for the PHS 398 (rev. 5/2001) at <http://grants.nih.gov/grants/funding/phs398/phs398.html> includes step-by-step guidance for preparing modular grants. Additional information on modular grants is available at <http://grants.nih.gov/grants/funding/modular/modular.htm>.

For the NIH Exploratory/Developmental Grant (R21), applicants may request direct costs in \$25,000 modules, up to a total direct cost of \$275,000 for the combined two year award period.

SENDING AN APPLICATION TO THE NIH: Submit a signed, typewritten original of the application, including the checklist, and five signed photocopies in one package to:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Room 1040, MSC 7710
Bethesda, MD 20892-7710
Bethesda, MD 20817 (for express/courier service)

APPLICATION PROCESSING: Applications must be received by or mailed on or before the receipt dates described at <http://grants.nih.gov/grants/funding/submissionschedule.htm>. The CSR will not accept any application in response to this PA that is essentially the same as one currently pending initial review unless the applicant withdraws the pending application. The CSR will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of a substantial revision of an R21 application already reviewed, but such application must include an Introduction addressing the previous critique.

Although there is no immediate acknowledgement of the receipt of an application, applicants are generally notified of the review and funding assignment within 8 weeks.

PEER REVIEW PROCESS

Applications submitted for this PA will be assigned on the basis of established PHS referral guidelines. An appropriate scientific review group, convened either by the relevant IC or by CSR in accordance with the standard NIH peer review procedures (<http://www.csr.nih.gov/refrev.htm>), will evaluate applications for scientific and technical merit.

As part of the initial merit review, all applications will:

- o Receive a written critique

- o Undergo a selection process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed and assigned a priority score
- o Receive a second level review by the appropriate national advisory council or board

REVIEW CRITERIA

The NIH R21 exploratory/developmental grant is a mechanism for supporting novel scientific ideas or new model systems, tools or technologies that have the potential to significantly advance our knowledge or the status of health-related research. Because the research plan is limited to 15 pages, an exploratory/developmental grant application need not have extensive background material or preliminary information as one might normally expect in an R01 application. Accordingly, reviewers will focus their evaluation on the conceptual framework, the level of innovation, and the potential to significantly advance our knowledge or understanding. Reviewers will place less emphasis on methodological details and certain indicators traditionally used in evaluating the scientific merit of R01 applications including supportive preliminary data. Appropriate justification for the proposed work can be provided through literature citations, data from other sources, or, when available, from investigator-generated data. Preliminary data are not required for R21 applications.

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In the written comments, reviewers will be asked to discuss the following aspects of the application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals:

- o Significance
- o Approach
- o Innovation
- o Investigator
- o Environment

The scientific review group will address and consider each of these criteria in assigning the application's overall score, weighting them as appropriate for each application. The application does not need to be strong in all categories to be judged likely to significantly advance current knowledge and thus deserve a meritorious priority score.

SIGNIFICANCE: Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effect of these studies on the concepts or methods that drive this field?

APPROACH: Are the conceptual framework, design, methods, and analyses adequately developed, well-integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

INNOVATION: Does the project employ novel concepts, approaches or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

INVESTIGATOR: Is the investigator appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers (if any)?

ENVIRONMENT: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

ADDITIONAL REVIEW CRITERIA: In addition to the above criteria, the following items will be considered in the determination of scientific merit and the priority score:

PROTECTION OF HUMAN SUBJECTS FROM RESEARCH RISK: The involvement of human subjects and protections from research risk relating to their participation in the proposed research will be assessed. (See criteria included in the section on Federal Citations, below).

INCLUSION OF WOMEN, MINORITIES AND CHILDREN IN RESEARCH: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research will be assessed. Plans for the recruitment and retention of subjects will also be evaluated. (See Inclusion Criteria in the sections on Federal Citations, below).

CARE AND USE OF VERTEBRATE ANIMALS IN RESEARCH: If vertebrate animals are to be used in the project, the five items described under Section f of the PHS 398 research grant application instructions (rev. 5/2001) will be assessed.

ADDITIONAL CONSIDERATIONS

BUDGET: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research.

AWARD CRITERIA

Applications submitted in response to this PA will compete for available funds with all other recommended applications. The following will be considered in making funding decisions:

- o Scientific merit of the proposed project as determined by peer review
- o Availability of funds
- o Relevance to program priorities

REQUIRED FEDERAL CITATIONS

HUMAN SUBJECTS PROTECTION: Federal regulations (45CFR46) require that applications and proposals involving human subjects must be evaluated with reference to the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained. <http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm>

MONITORING PLAN AND DATA SAFETY AND MONITORING BOARD: Research components involving Phase I and II clinical trials must include provisions for assessment of patient eligibility and status, rigorous data management, quality assurance, and auditing procedures. In addition, it is NIH policy that all clinical trials require data and safety monitoring, with the method and degree of monitoring being commensurate with the risks (NIH Policy for Data Safety and Monitoring, NIH Guide for Grants and Contracts, June 12, 1998: <http://grants.nih.gov/grants/guide/notice-files/not98-084.html>).

INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH: It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43).

All investigators proposing clinical research should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research - Amended, October, 2001," published in the NIH Guide for Grants and Contracts on October 9, 2001 (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html>); a complete copy of the updated Guidelines are available at

http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm.

The amended policy incorporates: the use of an NIH definition of clinical research; updated racial and ethnic categories in compliance with the new OMB standards; clarification of language governing NIH-defined Phase III clinical trials consistent with the new PHS Form 398; and updated roles and responsibilities of NIH staff and the extramural community. The policy continues to require for all NIH-defined Phase III clinical trials that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) investigators must report annual accrual and progress in conducting analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

INCLUSION OF CHILDREN AS PARTICIPANTS IN RESEARCH INVOLVING HUMAN SUBJECTS: The NIH maintains a policy that children (i.e., individuals under the age of 21) must be included in all human subjects research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them. This policy applies to all initial (Type 1) applications submitted for receipt dates after October 1, 1998.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the inclusion of children as participants in research involving human subjects that is available at <http://grants.nih.gov/grants/funding/children/children.htm>.

REQUIRED EDUCATION ON THE PROTECTION OF HUMAN SUBJECT PARTICIPANTS: NIH policy requires education on the protection of human subject participants for all investigators submitting NIH proposals for research involving human subjects. You will find this policy announcement in the NIH Guide for Grants and Contracts Announcement, dated June 5, 2000, at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html>.

HUMAN EMBRYONIC STEM CELLS (hESC): Criteria for federal funding of research on hESCs can be found at http://grants.nih.gov/grants/stem_cells.htm and at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html>. Only research using hESC lines that are registered in the NIH Human Embryonic Stem Cell Registry will be eligible for Federal funding (see <http://escr.nih.gov>). It is the responsibility of the applicant to provide the official NIH identifier(s) for the hESC line(s) to be used in the proposed research. Applications that do not provide this information will be returned without review.

PUBLIC ACCESS TO RESEARCH DATA THROUGH THE FREEDOM OF INFORMATION ACT: The Office of Management and Budget (OMB) Circular A-110 has been revised to provide public access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with Federal funds and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm.

Applicants may wish to place data collected under this PA in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

STANDARDS FOR PRIVACY OF INDIVIDUALLY IDENTIFIABLE HEALTH INFORMATION: The Department of Health and Human Services (DHHS) issued final modification to the "Standards for Privacy of Individually Identifiable Health Information", the "Privacy Rule," on August 14, 2002. The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information, and is

administered and enforced by the DHHS Office for Civil Rights (OCR). Those who must comply with the Privacy Rule (classified under the Rule as "covered entities") must do so by April 14, 2003 (with the exception of small health plans which have an extra year to comply).

Decisions about applicability and implementation of the Privacy Rule reside with the researcher and his/her institution. The OCR website (<http://www.hhs.gov/ocr/>) provides information on the Privacy Rule, including a complete Regulation Text and a set of decision tools on "Am I a covered entity?" Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding, and progress monitoring of grants, cooperative agreements, and research contracts can be found at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html>.

URLs IN NIH GRANT APPLICATIONS OR APPENDICES: All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

HEALTHY PEOPLE 2010: The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This PA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at <http://www.health.gov/healthypeople>.

AUTHORITY AND REGULATIONS: This program is described in the Catalog of Federal Domestic Assistance at <http://www.cfda.gov/> and is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The NIH Grants Policy Statement can be found at <http://grants.nih.gov/grants/policy/policy.htm>

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

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